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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/446,276	12/21/1999	YOSHIHISA NISHIBE	Q57234	2101

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SUGHRUE MION ZINN
MACPEAK & SEAS
2100 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20037-3202

EXAMINER

PULLIAM, AMY E

ART UNIT

PAPER NUMBER

1615

DATE MAILED: 07/11/2003

28

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/446,276

Applicant(s)

NISHIBE ET AL.

Examiner

Amy E Pulliam

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 5-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 5-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) : _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

Receipt of Papers

Receipt is acknowledged of the Extension of Time and the Request for Reconsideration, both received by the Office April 8, 2003.

Applicant's arguments have been fully considered but are not found to be persuasive in view of the following new rejections.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, and 5-30 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-30 of copending Application No. 10/201,303. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application

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since the referenced copending application and the instant application are claiming common subject matter, as follows:

Both Applications are drawn to an aqueous pharmaceutical composition for application to the mucosa, comprising one or more water insoluble and/ or water- low soluble substance, and one or more medicament, and having a low osmotic pressure. The '303 application is anticipated by the '276 application, because the '303 application requires an osmotic pressure of less than 290 mOsm, while the '276 application requires an osmotic pressure of less than 72 mOsm. Therefore, the teachings of the '276 application fall completely within the teachings of the '303 application, thus requiring a double patenting rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 5-10, and 13-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 496 308 to Craig *et al.* in view of JP 63-303931 to Osada *et al.*

Craig *et al.* teach a pharmaceutical composition in a form adapted for intranasal administration which comprises a suspension of an active agent. More specifically, Craig *et al.* teach that the suspensions will generally be aqueous, either being prepared by water alone, or water and a physiologically acceptable non-aqueous vehicle, such as polyethylene glycol (page

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2, lines 53-55). Craig *et al.* also teach that the suspensions may additionally contain other excipients, such as preservatives (benzalkonium chloride), surfactants (polysorbates such as Tween 80), isotonicity-adjusting agents (sodium chloride), and other additives (page 2, line 56 – page 2, line 1). Craig *et al.* also teach that the suspensions will be thickened by addition of a viscosity enhancer such as carboxymethylcellulose sodium, gelatin, guar gum, hydroxypropylmethyl cellulose, or methylcellulose (page 3, lines 5-7). The viscosity enhancer is preferably microcrystalline cellulose with sodium carboxymethylcellulose (page 3, lines 8-9). Craig *et al.* teaches the same components for their intranasal composition as Applicant's claimed composition.

Craig *et al.* does not disclose the particular osmolarity of their intranasal composition.

Osada *et al.* teach a drug preparation for application to the nasal mucosa. Osada *et al.* are relied upon for the teaching that an intranasal drug formulation has improved absorptivity of an active substance through the nasal mucosa into blood, exhibiting effective activity to release the active agent at a low rate of administration without accompanying harmful reaction. Osada *et al.* also teach that their formulation exhibits low toxicity and stimulation and is resistant to the decomposition of the active component. These improvements are achieved by suppressing the osmotic pressure ratio of an aqueous solution of the active substance to below a specific level, particularly less than 1, preferably between 0.3 and 0.1. [As discussed above, a ratio of 1 is equivalent to an osmotic pressure of 290 mOsm. Therefore, the preferably ratio discussed in the Osada *et al.* reference translates to 87 mOsm to 29 mOsm.] Therefore, the osmolarity discussed as preferably by Osada *et al.* clearly suggests the osmolarities claimed by Applicant.

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One skilled in the art would combine the teachings of Craig *et al.* and Osada *et al.*. Craig *et al.* teach an intranasal composition for the administration of an active agent into the nasal mucosa. Osada *et al.* teach that decreasing the osmolarity of a composition results in increase and improved absorption of the active through the nasal mucosa. One skilled in the art would rely on these teachings when preparing intranasal formulations, decreasing the osmolarity in order to improve absorption. The expected result would be successful intranasal composition with increased absorption and decreased toxicity. Therefore, this invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 2, 3, 28, 29, and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Craig *et al.* in view of Osada *et al.*.

Craig in view of Osada are discussed above as suggesting an aqueous suspension for intranasal administration of an active agent, with improved characteristics based upon the lowering of the osmotic pressure of the composition to below a particular value.

The combination of references does not teach the inclusion of a hemostatic agent. However, it is the position of the examiner that it would have been obvious to one of ordinary skill in the art to include a hemostatic agent in a intranasal mucosal formulation, so as to prevent any unwanted bleeding from the surface of the tender mucosal tissue. Absent any evidence to the contrary, the examiner sees no criticality placed on the presence of a hemostatic agent in the formulation. It appears that the use of a hemostatic agent is no more than addition of another well known active into the formulation. Furthermore, the selection of a known material

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based on its suitability for its intended use is obvious absent a clear showing of unexpected results attributable to the Applicant's specific selection. Therefore, this limitation does not add patentable distinction to the claimed invention, and this invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Craig *et al.* in view of Osada *et al.* and further in view of US Patent 5,281,580 to Yamamoto *et al.*

The combination of references does not specifically teach the use of glucose as an osmotic controlling agent.

Yamamoto *et al.* teaches an aqueous liquid formulation for nasal administration. Yamamoto *et al.* are relied upon for the teaching that both sodium chloride and glucose are known to help in controlling the osmotic pressure of a liquid composition.

One of ordinary skill in the art would have been motivated to use any well known osmotic controlling agent, such as either sodium chloride or glucose, when attempting to alter the osmotic pressure of a particular formulation. Therefore, this limitation does not render patentability to the present invention, and the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E Pulliam whose telephone number is 703-308-4710. The examiner can normally be reached on Mon-Thurs 7:30-5:00, Alternate Fri 8:30-5:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

A, Pulliam
Patent Examiner
Art Unit 1615
July 10, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600